10/537940
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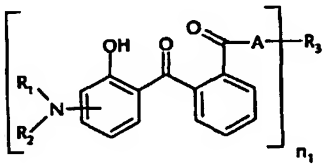
Amino substituted hydroxyphenyl benzophenone derivatives

The present invention relates to amino substituted hydroxyphenyl benzophenone derivatives, the process for the preparation of these compounds, the use of these UV absorbers, preferably for the protection of human and animal hairs and from the damage of UV radiation as well as cosmetic compositions comprising these compounds.

The new compounds correspond to the formula

(1)  , wherein

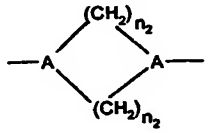
R_1 and R_2 independently from each other are; C_1-C_{20}alkyl; C_2-C_{20}alkenyl; C_3-C_{10}cycloalkyl; C_3-C_{10}cycloalkenyl; or R_1 and R_2 together with the linking nitrogen atom form a 5- or 6-membered heterocyclic ring;

n_1 is a number from 1 to 4;

when n_1 = 1,

R_3 is a saturated or unsaturated heterocyclic radical; hydroxy-C_1-C_5alkyl; cyclohexyl optionally substituted with one or more C_1-C_5alkyl; phenyl optionally substituted with a heterocyclic radical, aminocarbonyl or C_1-C_5alkylcarboxy;

when n_1 is 2,

R_3 is an alkylene-, cycloalkylene, alkenylene or phenylene radical which is optionally substituted by a carbonyl- or carboxy group; a radical of formula $\bullet-CH_2-C\equiv C-CH_2-\bullet$ or R_3 together with A forms a bivalent radical of the formula (1a)  ; wherein

n_2 is a number from 1 to 3;

when n_1 is 3,

R_3 is an alkantriyl radical;

wenn n_1 is 4,

R_3 is an alkantetrayl radical;

A is -O-; or $-N(R_5)-$; and

R_5 is hydrogen; C_1-C_5alkyl; or hydroxy-C_1-C_5alkyl.

C_1-C_{20}Alkyl denotes a linear or branched, unsubstituted or substituted alkyl group such as, for example, methyl, ethyl, propyl, isopropyl, n-butyl, n-hexyl, cyclohexyl, n-decyl, n-dodecyl, n-octadecyl, eicosyl, methoxyethyl, ethoxypropyl, 2-ethylhexyl, hydroxyethyl, chloropropyl, N,N-diethylaminopropyl, cyanoethyl, phenethyl, benzyl, p-tert-butylphenethyl, p-tert-octyl-phenoxyethyl, 3-(2,4-di-tert-amylphenoxy)-propyl, ethoxycarbonylmethyl-2-(2-hydroxy-ethoxy)ethyl or 2-furylethyl.

C_2-C_{20}alkenyl is for example allyl, methallyl, isopropenyl, 2-butenyl, 3-butenyl, isobutenyl, n-penta-2,4-dienyl, 3-methyl-but-2-enyl, n-oct-2-enyl, n-dodec-2-enyl, iso-dodecenyl, n-dodec-2-enyl or n-octadec-4-enyl.

C_3-C_{10}cycloalkyl is for example cyclopropyl, cyclobutyl, cyclopentyl, cycloheptyl, cyclooctyl, cyclononyl or cyclodecyl and preferably cyclohexyl. These radicals may besubstituted, for example by one or more oder equal or different C_1-C_4alkyl radicals, preferably by methyl, and/or hydroxy. If cycloalkyl radicals are substituted by one or more radicals, they are preferably substituted by one, two or four, preferably by one or two equal or radicals.

C_3-C_{10}cycloalkenyl is for example cyclopropenyl, cyclobutenyl, cyclopentenyl, cycloheptenyl, cycloocentyl, cyclononenyl or cyclodecenyl and preferably cyclohexenyl. These radicals may be substituted with one or more equal or different C_1-C_4alkyl radical, preferably with methyl, and/or hydroxy. If cycloalkenyl radicals are substituted with one or more radicals they are preferably substituted with one, two, three or four, preferably with one or two equal or different radicals.

Hydroxy substituted C_1-C_5alkyl groups are for example hydroxymehtyl, hydroxyethyl, hydroxypropyl, hydroxybutyl or hydroxypentyl.

An alkiyene radical is preferably a C_1-C_{12}alkylene radical, like for example methylene, ethylene, propylene, butylene, hexylene or octylene.

The alkiyene radicals may optionally be substituted by one or more C_1-C_5alkyl radicals.

If R_1 and R_2 are heterocyclic radicals, these comprise one, two, three or four equal or different ring hetero atoms. Special preference is given to heterocycles which contain one, two or three, especially one or two, identical or different hetero atoms. The heterocycles may be mono- or poly-cyclic, for example mono-, bi- or tri-cyclic. They are preferably mono- or bi-cyclic, especially monocyclic. The rings preferably contain 5, 6 or 7 ring members. Examples of monocyclic and bicyclic heterocyclic systems from which radicals occurring in the compounds of formula (1) or (2) may be derived are, for example, pyrrole, furan, thiophene, imidazole, pyrazole, 1,2,3-triazole, 1,2,4-triazole, pyridine, pyridazine, pyrimidine, pyrazine, pyran, thiopyran, 1,4-dioxane, 1,2-oxazine, 1,3-oxazine, 1,4-oxazine, indole, benzothiophene, benzofuran, pyrrolidine, piperidine, piperazine, morpholine and thiomorpholine.

Preference is given to compounds of formula (1), wherein

R_1 and R_2 independently from each other are hydrogen; C_1-C_{20}alkyl; C_2-C_{20}alkenyl; C_3-C_{10}cycloalkyl; C_3-C_{10}cycloalkenyl; or R_1 and R_2 together with the linking nitrogen atom form a 5- or 6-membered heterocyclic ring;

n_1 is a number from 1 to 4;

wenn n_1 is 1,

R_3 is a saturated or unsaturated heterocyclic radical; hydroxy-C_1-C_5alkyl; Cyclohexyl substituted with one or more C_1-C_5alkyl;

wenn n_1 is 2,

R_3 is an alkylene-, cycloalkylene- or alkenylene radical which is optionally interrupted by a carbonyl- or carboxy group;

wenn n_1 is 3,

R_3 is an alkantriyl radical;

wenn n_1 is 4,

R_3 is an alkanetetrayl radical;

A is -O-; or $-N(R_5)-$; and

R_5 is hydrogen; C_1-C_5alkyl; or hydroxy-C_1-C_5alkyl.

Of preferred interest are compounds of formula (1), wherein

R_1 and R_2 are C_1-C_{20}alkyl, preferably C_1-C_5alkyl; and most preferably ethyl.

Preferably R_1 and R_2 in formula (1) have the same definition.

If in formula (1) n_1 is 1, compounds are preferred, wherein

R_3 is a saturated or unsaturated heterocyclic radical, most preferably a saturated heterocyclic radical.

Among these compounds are those preferred, wherein

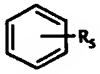
R_3 is a monocyclic radical of 5, 6 or 7 ring members with one or more heteroatoms, preferably wherein

R_3 is morphonlinyl; piperazinyl; piperidyl; pyrazolidinyl; imadazolidinyl; or pyrrolidinyl.

When n_1 is 1 further compounds of formula (1) are of interest wherein

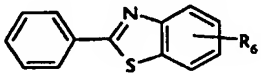
R_3 is an unsaturated heterocyclic radical, preferably a polycyclic radical.

Most preferred are compounds of formula (1), wherein

R_3 is a radical of formula (1a)  , and

R_5 is polycyclic heteroaromatic radical with one or 2 heteroatoms.

Of preferred interest are compounds of formula (1), wherein

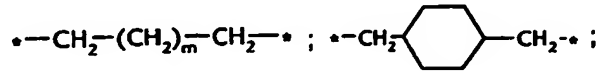
R_3 is a radical of formula (1b)  , wherein

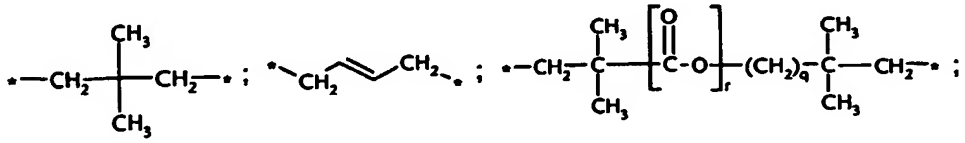
R_6 is hydrogen; or C_1-C_5alkyl.

If n_1 is 2,

R_3 is preferably a C_1-C_{12}alkylene radical, most preferably a C_2-C_8alkylene radical.

Mostly preferred are compounds of formula (1), wherein

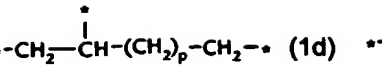
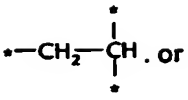
R_3 is a radical of formula  ;

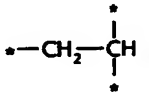
 ;

r is 0 or 1; and

q = is a number from 0 to 5.

If in formula (1) n_1 is 3,

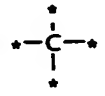
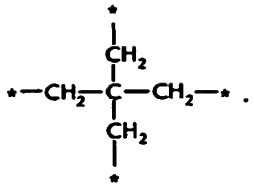
R_3 is preferably a radical of formula (1c)  (1d)  . or

(1e)  and

p is a number from 0 to 3.

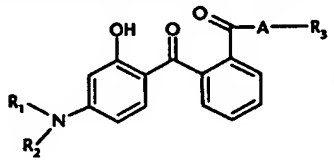
R_1, R_2 and A are defined as in formula (1).

If in formula (1) n_1 is 4,

R_3 is a radical of formula  ; or  .

R_1, R_2 and A are defined as in formula (1).

Preferred compounds of the present invention correspond to formula

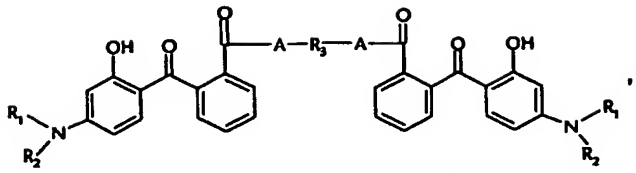
(2)  , wherein

R_1 and R_2 independently from each other are hydrogen; or C_1-C_5alkyl;

A is -NH; or –O-; and

R_3 is a saturated or unsaturated heterocyclic radical.

Furthermore compounds of the present invention are preferred which correspond to formula

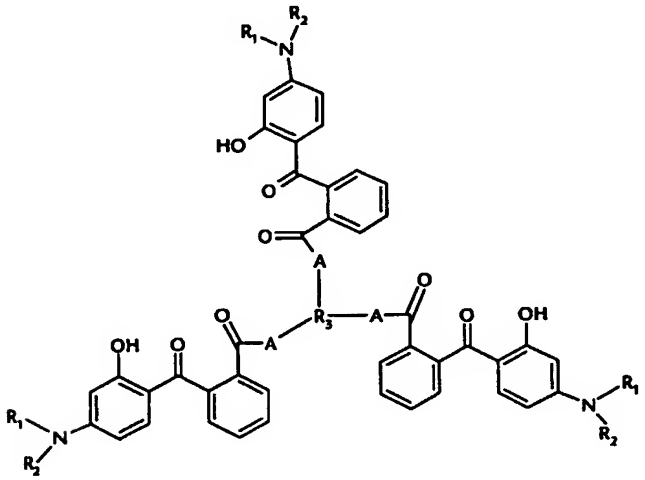
(3)  , wherein

R_1 and R_2 independently from each other are hydrogen; or C_1-C_5alkyl;

A is -NH; or –O-; and

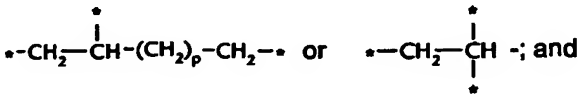
R_3 is a C_1-C_{12}alkylene radical.

Preferred are also compounds of formula

(4)  , wherein

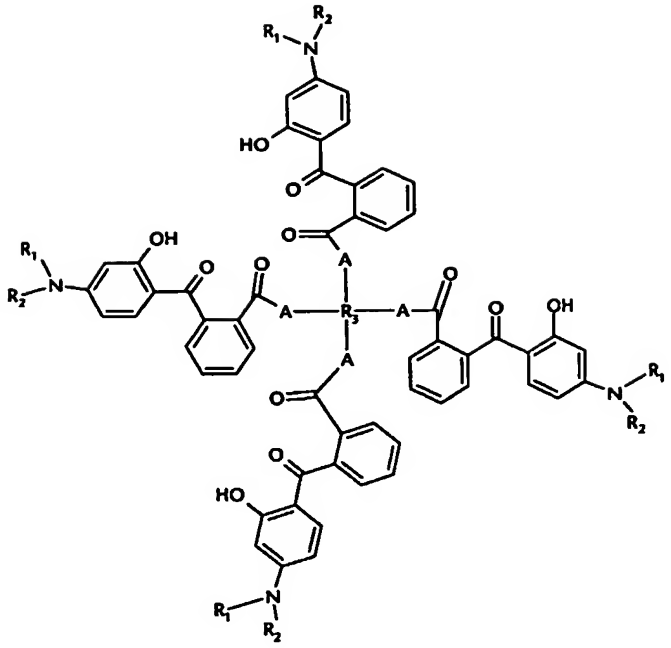
R_1 and R_2 independently from each other are hydrogen; or C_1-C_5alkyl;

A is -NH; or –O-;

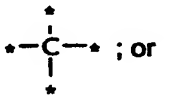
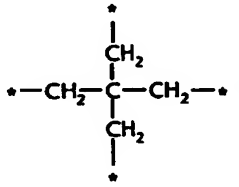
R_3 is  ; and

p is a number from 0 to 3.

Furthermore, compounds of formula

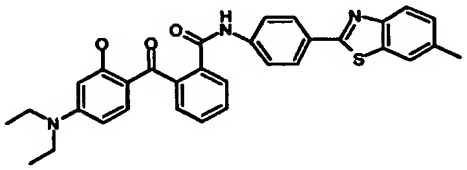
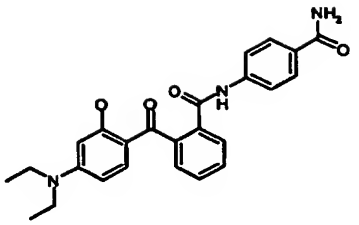
(5) 

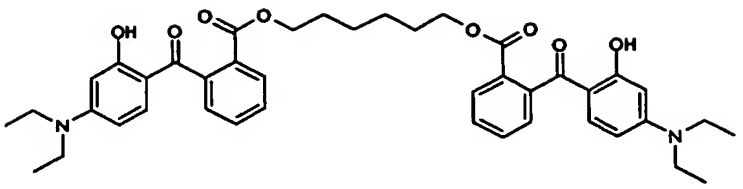
are preferred, wherein

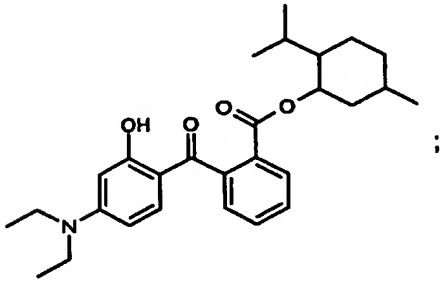
R_3 is a radical of formula  ; or  ; and

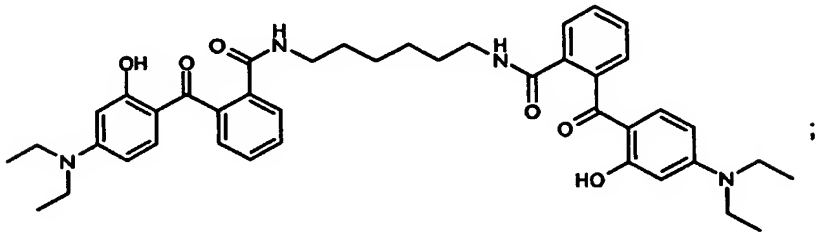
R_1, R_2 and A are defined as in formula (1).

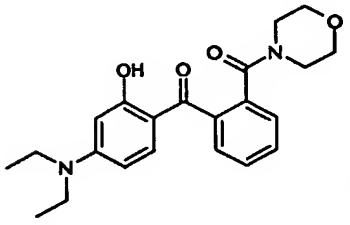
Exemplified compounds of the present invention are of formulae

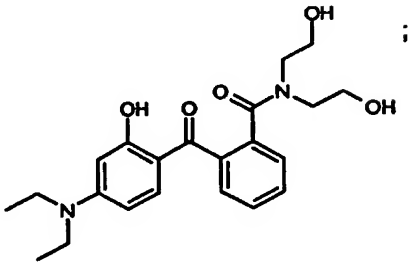
(HPB1)  ; (HPB2)  ;

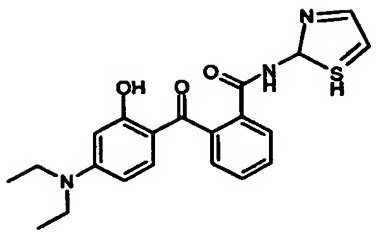
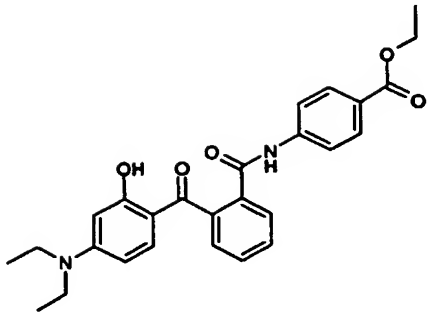
(HPB3)  ;

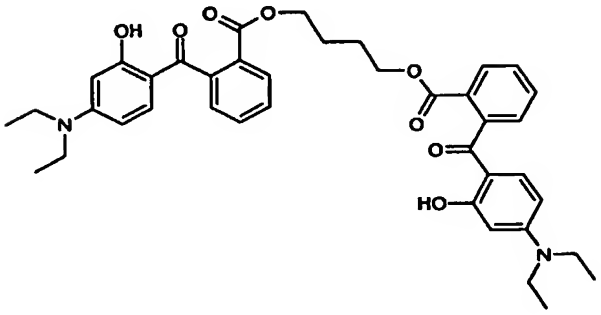
(HPB4)  ;

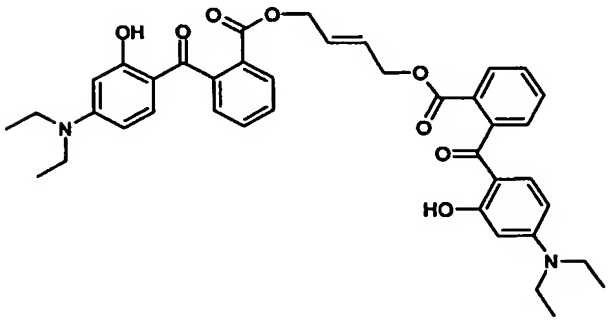
(HPB5)  ;

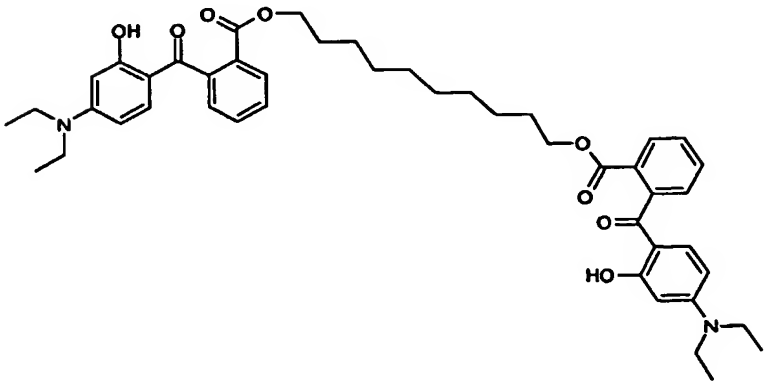
(HPB6) 

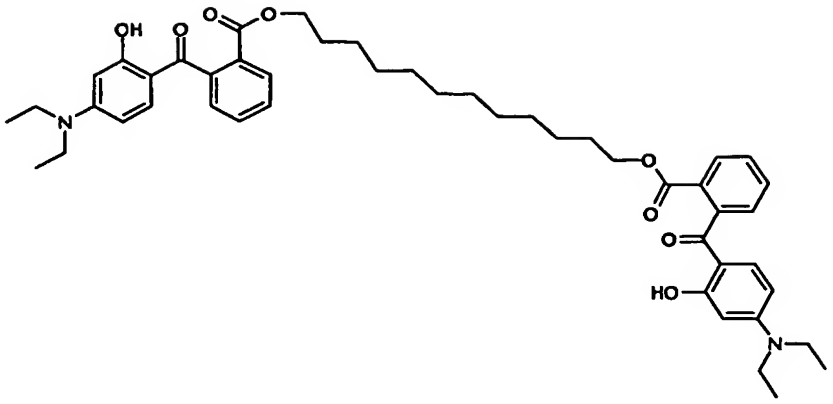
(HPB7)  ;

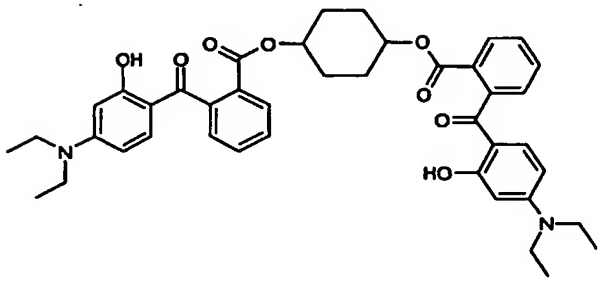
(HPB8)  ; (HPB9)  ;

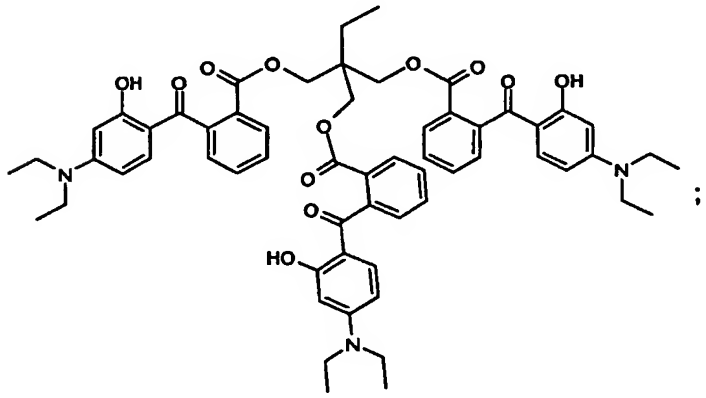
(HPB10)  ;

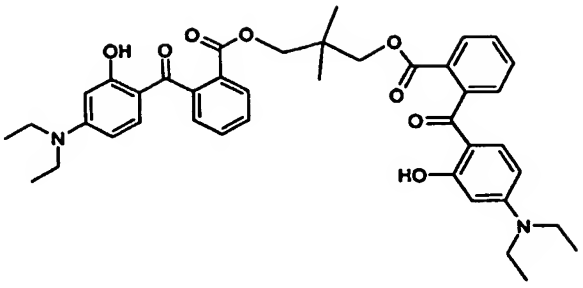
(HPB11)  ;

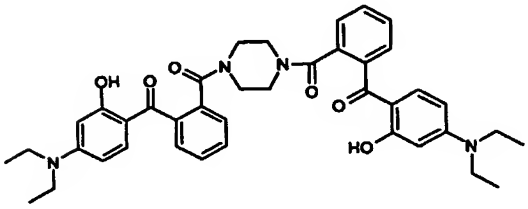
(HPB12)  ;

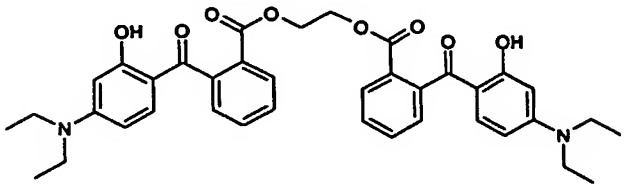
(HPB13)  ;

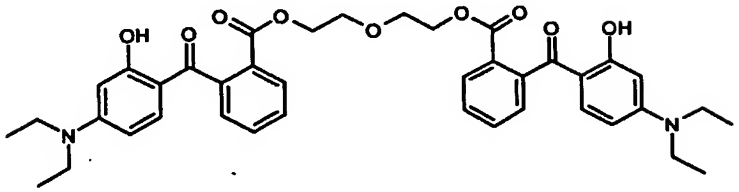
(HPB14)  ;

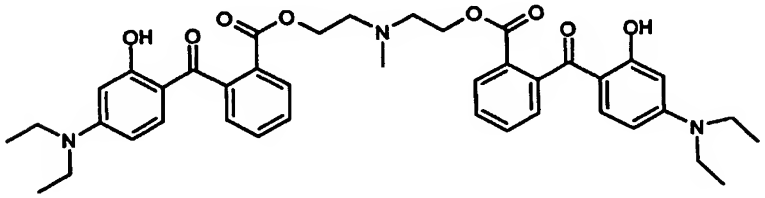
(HPB15)  ;

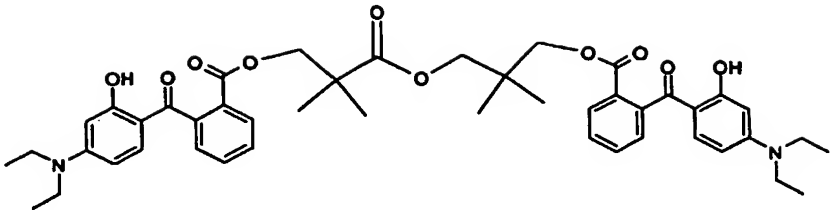
(HPB16)  ;

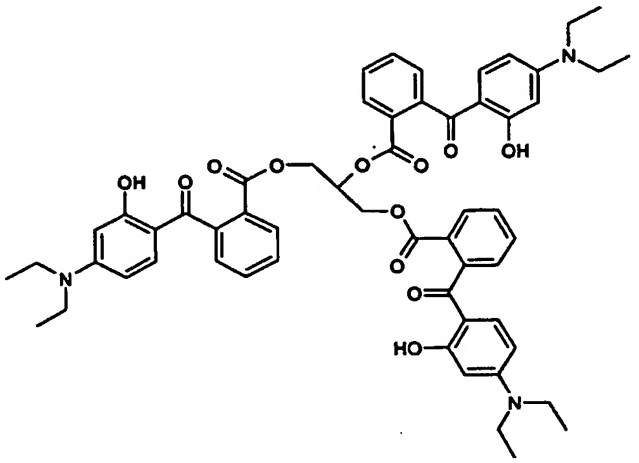
(HPB17) 

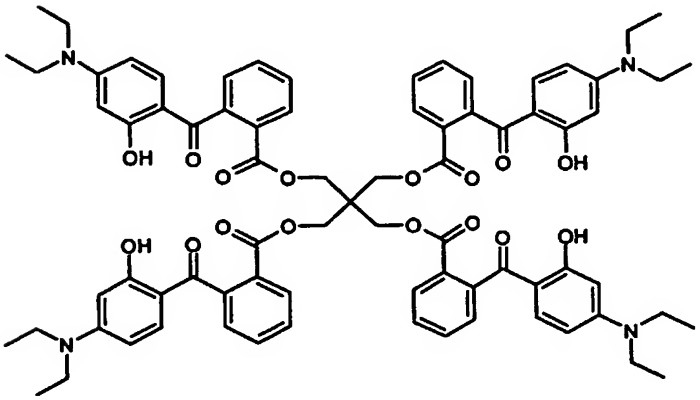
(HPB18) 

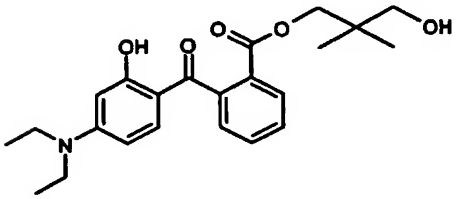
(HPB20)  ;

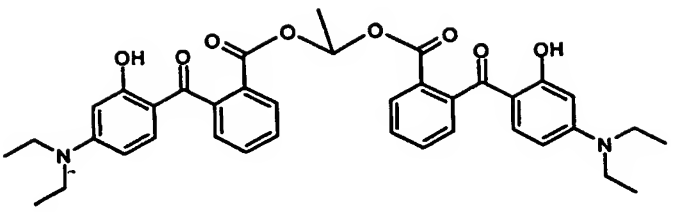
(HPB21)  ;

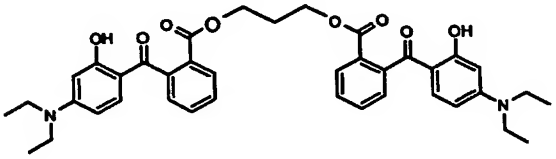
(HPB22)  ;

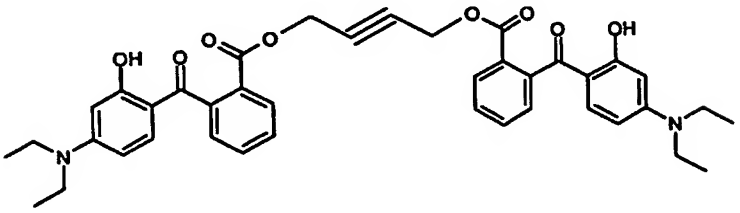
(HPB23)  ;

(HPB24) 

(HPB25)  ;

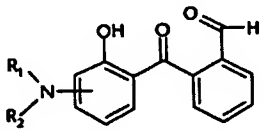
(HPB26)  ;

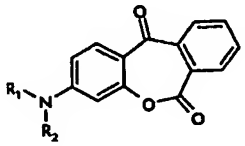
(HPB27)  ; and

(HPB28)  .

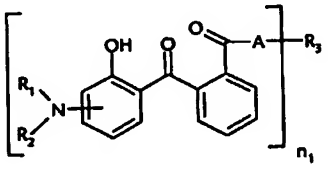
The compounds of formula (1) may be prepared according to known methods as described for example in EP-1,046,391.

Preferably, the compounds formula (1) are prepared by

(a) dehydratisation of formula (6a)  to the compound of formula

(6b)  and

(b) reacting the obtained anhydride with the compound ($4c_1$) H-N(R_4)-R_3 or H-O-R_3 to the compound of formula

(1)  , wherein

R_1 and R_2 independently from each other are hydrogen; C_1-C_{20}alkyl; C_2-C_{20}alkenyl; C_3-C_{10}cycloalkyl; C_3-C_{10}cycloalkenyl; or R_1 and R_2 together with the linking nitrogen atom form a 5- or 6-membered heterocyclic ring;

n_1 is 1 to 4;

when n_1 is 1,

R_3 is hydrogen; C_1-C_{20}alkyl; hydroxy-C_1-C_5alkyl; C_2-C_{20}alkenyl; C_3-C_{10}-Cyclohexyl whis is not substituted or substituted by one or more C_1-C_5alkyl; $(Y\text{-}O)_pZ$; C_6-C_{10}aryl; or a saturated or unsaturated heterocyclic radical;

Y is C_1-C_{12}alkylene;

Z is C_1-C_5alkyl;

p is a number from 1 to 20;

if n_1 is 2,

R_3 is an alkylene-, cycloalkylene- or alkenylene radical which is optionally interrupted by carbonyl- or carboxy group;

if n_1 is 3,

R_3 is an alkantriyl radical;

if n_1 is 4,

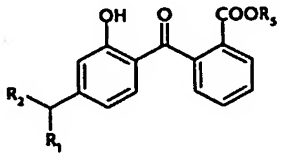
R_3 is a alkantetrayl radical;

A is -O-; or $-N(R_5)$-;

R_5 is hydrogen; C_1-C_5alkyl; or hydroxy-C_1-C_5alkyl; and

R_5 is hydrogen; C_1-C_5alkyl; or hydroxy-C_1-C_5alkyl.

The process for the preparation is a further object of the present invention.

Preferably compounds of formula (7) 

, wherein

R_1 and R_2 independently from each other are C_1-C_{12}alkyl; and

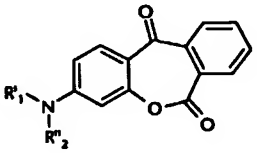
R_5 is hydrogen; C_1-C_{12}alkyl; or C_3-C_6cycloalkyl;

can be obtained according to the process of the present invention.

The reaction is usually carried out at a temperature from 25 to 200°C, preferably at room temperature. Generally a solvent is not necessary for this reaction step. If a solvent is used however, preferably the solvents as used in the working examples are preferred.

The compounds of formula (1) may be easily recrystallized as x-HCl-salts.

The intermediates of formula

(6b')  , wherein

R_1' and R_2" independently from each other are hydrogen; C_1-C_{20}alkyl; C_2-C_{20}alkenyl; C_3-C_{10}cycloalkyl; C_3-C_{10}cycloalkenyl; or R_1 and R_2 together with the lining nitrogen atom form a 5- or 6-membered heterocyclic ring;

are compounds not known from the prior art.

They represent starting compounds for the preparation of organic UV filters.

The compounds of formula (6b') are a further object of the present invention.

The compounds of formula (1) are suitable especially as UV filters, that is to say for the protection of organic materials that are sensitive to ultraviolet light, especially human and animal skin and hair, against the action of UV radiation. Such compounds are accordingly suitable as light-protective agents in cosmetic, pharmaceutical and veterinary medicine preparations.

A further object of the present invention is therefore a cosmetic preparation comprising at least one of the compounds of formula (1) together with cosmetically acceptable carriers or adjuvants.

The UV absorbers according to the present invention can be used either in the dissolved state (soluble organic filters, solubilised organic filters) or in the micronised state (nanoscalar organic filters, particulate organic filters, UV-absorber pigments).

Any known process suitable for the preparation of microparticles can be used for the preparation of the micronised UV absorbers, for example:

- wet-milling (low-viscosity micronisation process for pumpable dispersions), with a hard grinding medium, for example zirconium silicate balls in a ball mill, and a protective surfactant or a protective polymer in water or in a suitable organic solvent;
- wet-kneading (high-viscosity micronisation process for non-pumpable pastes) using a continuous or discontinuous (batch) kneader. For a wet-kneading process, a solvent (water or cosmetically acceptable oils), a grinding aid (surfactant, emulsifier) and a polymeric grinding aid may be used.

Both processes may be used preferably.

- spray-drying from a suitable solvent, for example aqueous suspensions or suspensions containing organic solvents, or true solutions in water, ethanol, dichloroethane, toluene or N-methylpyrrolidone etc..
- by expansion according to the RESS process (Rapid Expansion of Supercritical Solutions) of supercritical fluids (e.g. CO_2) in which the UV filter or filters is/are dissolved, or the expansion of liquid carbon dioxide together with a solution of one or more UV filters in a suitable organic solvent;
- by reprecipitation from suitable solvents, including supercritical fluids (GASR process = Gas Anti-Solvent Recrystallisation / PCA process = Precipitation with Compressed Anti-solvents).

As milling apparatus for the preparation of the micronised organic UV absorbers there may be used, for example, a jet mill, ball mill, vibratory mill or hammer mill, preferably a high-speed mixing mill. Even more preferable mills are modern ball mills; manufacturers of these types of mill are, for example, Netzsch (LMZ mill), Drais (DCP-Viscoflow or Cosmo), Bühler AG (centrifugal mills) or Bachhofer. The grinding is preferably carried out with a grinding aid.

Examples of kneading apparatus for the preparation of the micronised organic UV absorbers are typical sigma-blade batch kneaders but also serial batch kneaders (IKA-Werke) or continuous kneaders (Continua from Werner und Pfleiderer).

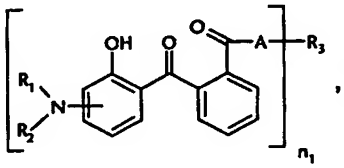
Useful low molecular weight grinding aids for all the above micronisation processes are dispersing agents and surfactants and emulsifiers as disclosed below in the sections entitled "Emulsifiers", "Surfactants" and "Fatty alcohols".

Useful polymeric grinding aids for water dispersion are cosmetically acceptable water-soluble polymers with Mn > 500 g/mol, for example: acrylates (Salcare types), modified or non-modified polysaccharides, polyglucosides or xanthan gum. Furthermore an alkylated vinyl-pyrrolidone polymer, a vinylpyrrolidone/vinyl acetate copolymer, an acyl glutamate, an alkyl polyglucoside, Ceteareth-25 or a phospholipid may be used. Oil dispersions may comprise cosmetically acceptable waxy polymers or natural waxes as polymeric grinding aid to adjust the viscosity during and after processing. Examples of other useful polymeric grinding aids are disclosed below in the section entitled "Polymers".

Useful solvents are water, brine, (poly-)ethylene glycol, glycerol or cosmetically acceptable oils. Other useful solvents are disclosed below in the sections entitled "Esters of fatty acids", "Natural and synthetic triglycerides, including glyceryl esters and derivatives", "Pearlescent waxes", "Hydrocarbon oils" and "Silicones or siloxanes".

The micronised UV absorbers so obtained usually have an average particle size from 0.02 to 2 micrometres, preferably from 0.03 to 1.5 micrometres and more especially from 0.05 to 1.0 micrometres.

A further object of the present invention is a UV absorber dispersion, comprising
(a) a micronised UV absorber of formula

(1')  , wherein

R_1 and R_2 independently from each other are hydrogen; C_1-C_{20}alkyl; C_2-C_{20}alkenyl; C_3-C_{10}cycloalkyl; C_3-C_{10}cycloalkenyl; or R_1 and R_2 together with the linking nitrogen atom form a 5- or 6-membered heterocyclic ring;

when n_1 is 1,

R_3 is hydrogen; C_1-C_{20}alkyl; hydroxy-C_1-C_5alkyl; C_2-C_{20}alkenyl; not substituted or with one or more C_1-C_5alkyl substituted C_3-C_{10}cyclohexyl; $(Y\text{-}O)_pZ$; C_6-C_{10}aryl; or a saturated or unsaturated heterocyclic radical;

Y C_1-C_{12}alkylen;

Z C_1-C_5alkyl;

p is a number from 1 to 20;

when n_1 is 2,

R_3 is a alkylen-, cycloalkylen- or alkenylen- radical optionally interrupted by a carbonyl- or carboxy group;

if n_1 is,

R_3 is an alkantriyl radical;

if n_1 is 4,

R_3 is an alkantetrayl radical;

A is -O-; or –N(R_5)-; and

R_5 is hydrogen; C_1-C_5alkyl; or hydroxy-C_1-C_5alkyl;

R_5 is hydrogen; C_1-C_5alkyl; or hydroxy-C_1-C_5Alkyl;

Having a particle size from 0,02 to 2 µm, and

(b) a suitable dispersing agent.

The UV absorbers according to the present invention can also be used dry in powder form. For that purpose, the UV absorbers are subjected to known grinding methods, such as vacuum atomisation, countercurrent spray-drying etc.. Such powders have a particle size of from 0.1 micrometers to 2 micrometers. To avoid the occurrence of agglomeration, the UV absorbers can be coated with a surface-active compound prior to the pulverisation process, for example with an anionic, non-ionic or amphoteric surfactant, e.g. a phospholipid or a known polymer, such as PVP, an acrylate etc..

The UV absorbers according to the present invention can also be used in specific carriers for cosmetics, for example in solid lipid nanoparticles (SLN) or in inert sol-gel microcapsules wherein the UV absorbers are encapsulated.

The cosmetic formulations or pharmaceutical compositions according to the present invention can also comprise one or more than one further UV filter.

The cosmetic or pharmaceutical preparations can be prepared by physically mixing the UV absorber(s) with the adjuvant using customary methods, for example by simply stirring together the individual components, especially by making use of the dissolution properties of already known cosmetic UV absorbers, for example octyl methoxycinnamate, salicylic acid

isooctyl ester etc.. The UV absorber can be used, for example, without further treatment, or in the micronised state, or in the form of a powder.

Cosmetic or pharmaceutical preparations contain from 0.05 % to 40 % by weight, based on the total weight of the composition, of one UV absorber or a mixture of UV absorbers.

Preference is given to the use of mixing ratios of the UV absorber of formula (1) according to the present invention and optional further light-protective agents of from 1:99 to 99:1, especially from 1:95 to 95:1 and preferably from 10:90 to 90:10, based on weight. Of special interest are mixing ratios of from 20:80 to 80:20, especially from 40:60 to 60:40 and preferably approximately 50:50. Such mixtures can be used, *inter alia*, to improve solubility or increase UV absorption.

The UV absorbers of formula (1) according to the present invention or combinations of UV filters are useful for protecting skin, hair and/or natural or artificial hair colour.

Suitable UV filter substances which can additionally be used with the UV absorbers according to the present invention are any UV-A and UV-B filter substances.

The cosmetic or pharmaceutical preparations may be, for example, creams, gels, lotions, alcoholic and aqueous/alcoholic solutions, emulsions, wax/fat compositions, stick preparations, powders or ointments. In addition to the above-mentioned UV filters, the cosmetic or pharmaceutical preparations may contain further adjuvants as described below.

As water- and oil-containing emulsions (e.g. W/O, O/W, O/W/O and W/O/W emulsions or microemulsions) the preparations contain, for example, from 0.1 to 30 % by weight, preferably from 0.1 to 15 % by weight and especially from 0.5 to 10 % by weight, based on the total weight of the composition, of one or more UV absorbers, from 1 to 60 % by weight, especially from 5 to 50 % by weight and preferably from 10 to 35 % by weight, based on the total weight of the composition, of at least one oil component, from 0 to 30 % by weight, especially from 1 to 30 % by weight und preferably from 4 to 20 % by weight, based on the total weight of the composition, of at least one emulsifier, from 10 to 90 % by weight, especially from 30 to 90 % by weight, based on the total weight of the composition, of water, and from 0 to 88.9

% by weight, especially from 1 to 50 % by weight, of further cosmetically acceptable adjuvants.

The cosmetic or pharmaceutical compositions/preparations according to the invention may also comprise one or one more additional compounds as described below, for example fatty alcohols, esters of fatty acids, natural or synthetic triglycerides, including glyceryl esters and derivatives Pearlescent waxes, Hydrocarbon oils, silicones or siloxanes (organo-substituted polysiloxanes), fluorinated or perfluorinated oils,emulsifiers, adjuvants and additives, uperfatting agents, surfactants, consistency regulators/thickeners and rheology modifiers, polymers, anti-dandruff agents, film formers, antioxidants, hydrotropic agents, preservatives and bacteria-inhibiting agents, perfume oils, colorants, or polymeric beads or hollow spheres as SPF enhancers

Cosmetic or pharmaceutical preparations

Cosmetic or pharmaceutical formulations are contained in a wide variety of cosmetic preparations. There come into consideration, for example, especially the following preparations:

- skin-care preparations, e.g. skin-washing and cleansing preparations in the form of tablet-form or liquid soaps, soapless detergents or washing pastes;
- bath preparations, e.g. liquid (foam baths, milks, shower preparations) or solid bath preparations, e.g. bath cubes and bath salts;
- skin-care preparations, e.g. skin emulsions, multi-emulsions or skin oils;
- cosmetic personal care preparations, e.g. facial make-up in the form of day creams or powder creams, face powder (loose or pressed), rouge or cream make-up, eye-care preparations, e.g. eyeshadow preparations, mascara, eyeliner, eye creams or eye-fix creams; lip-care preparations, e.g. lipsticks, lip gloss, lip contour pencils, nail-care preparations, such as nail varnish, nail varnish removers, nail hardeners or cuticle removers;
- foot-care preparations, e.g. foot baths, foot powders, foot creams or foot balsams, special deodorants and antiperspirants or callus-removing preparations;
- light-protective preparations, such as sun milks, lotions, creams or oils, sunblocks or tropicals, pre-tanning preparations or after-sun preparations;
- skin-tanning preparations, e.g. self-tanning creams;

- depigmenting preparations, e.g. preparations for bleaching the skin or skin-lightening preparations;
- insect-repellents, e.g. insect-repellent oils, lotions, sprays or sticks;
- deodorants, such as deodorant sprays, pump-action sprays, deodorant gels, sticks or roll-ons;
- antiperspirants, e.g. antiperspirant sticks, creams or roll-ons;
- preparations for cleansing and caring for blemished skin, e.g. synthetic detergents (solid or liquid), peeling or scrub preparations or peeling masks;
- hair-removal preparations in chemical form (depilation), e.g. hair-removing powders, liquid hair-removing preparations, cream- or paste-form hair-removing preparations, hair-removing preparations in gel form or aerosol foams;
- shaving preparations, e.g. shaving soap, foaming shaving creams, non-foaming shaving creams, foams and gels, preshave preparations for dry shaving, aftershaves or aftershave lotions;
- fragrance preparations, e.g. fragrances (eau de Cologne, eau de toilette, eau de parfum, parfum de toilette, perfume), perfume oils or perfume creams;
- cosmetic hair-treatment preparations, e.g. hair-washing preparations in the form of shampoos and conditioners, hair-care preparations, e.g. pretreatment preparations, hair tonics, styling creams, styling gels, pomades, hair rinses, treatment packs, intensive hair treatments, hair-structuring preparations, e.g. hair-waving preparations for permanent waves (hot wave, mild wave, cold wave), hair-straightening preparations, liquid hair-setting preparations, hair foams, hairsprays, bleaching preparations, e.g. hydrogen peroxide solutions, lightening shampoos, bleaching creams, bleaching powders, bleaching pastes or oils, temporary, semi-permanent or permanent hair colourants, preparations containing self-oxidising dyes, or natural hair colourants, such as henna or camomile.

Presentation forms

The final formulations listed may exist in a wide variety of presentation forms, for example:

- in the form of liquid preparations as a W/O, O/W, O/W/O, W/O/W or PIT emulsion and all kinds of microemulsions,
- in the form of a gel,
- in the form of an oil, a cream, milk or lotion,

- in the form of a powder, a lacquer, a tablet or make-up,
- in the form of a stick,
- in the form of a spray (spray with propellent gas or pump-action spray) or an aerosol,
- in the form of a foam, or
- in the form of a paste.

Of special importance as cosmetic preparations for the skin are light-protective preparations, such as sun milks, lotions, creams, oils, sunblocks or tropicals, pretanning preparations or after-sun preparations, also skin-tanning preparations, for example self-tanning creams. Of special interest are sun protection creams, sun protection lotions, sun protection milk and sun protection preparations in the form of a spray.

Of special importance as cosmetic preparations for the hair are the above-mentioned preparations for hair treatment, especially hair-washing preparations in the form of shampoos, hair conditioners, hair-care preparations, e.g. pretreatment preparations, hair tonics, styling creams, styling gels, pomades, hair rinses, treatment packs, intensive hair treatments, hair-straightening preparations, liquid hair-setting preparations, hair foams and hairsprays. Of special interest are hair-washing preparations in the form of shampoos.

A shampoo has, for example, the following composition: from 0.01 to 5 % by weight of a UV absorber according to the invention, 12.0 % by weight of sodium laureth-2-sulfate, 4.0 % by weight of cocamidopropyl betaine, 3.0 % by weight of sodium chloride, and water ad 100%.

For example, especially the following hair-cosmetic formulations may be used:

a_1) spontaneously emulsifying stock formulation, consisting of the UV absorber according to the invention, PEG-6-C_{10}oxoalcohol and sorbitan sesquioleate, to which water and any desired quaternary ammonium compound, for example 4 % minkamidopropyl dimethyl-2-hydroxyethylammonium chloride or Quaternium 80, is added;

a_2) spontaneously emulsifying stock formulation consisting of the UV absorber according to the invention, tributyl citrate and PEG-20-sorbitan monooleate, to which water and any desired quaternary ammonium compound, for example 4 % minkamidopropyl dimethyl-2-hydroxyethylammonium chloride or Quaternium 80, is added;

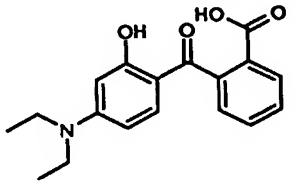
b) quat-doped solutions of the UV absorber according to the invention in butyl triglycol and tributyl citrate;

c) mixtures or solutions of the UV absorber according to the invention with n-alkylpyrrolidone.

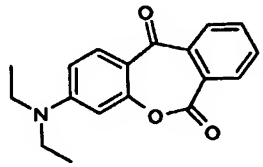
Other typical ingredients in such formulations are preservatives, bactericides and bacteriostatic agents, perfumes, dyes, pigments, thickening agents, moisturising agents, humectants, fats, oils, waxes or other typical ingredients of cosmetic and personal care formulations such as alcohols, poly-alcohols, polymers, electrolytes, organic solvents, silicon derivatives, emollients, emulsifiers or emulsifying surfactants, surfactants, dispersing agents, antioxidants, anti-irritants and anti-inflammatory agents etc..

Preparation of new compounds

Example 1: Preparation of 3-diethylamino-dibenzo-oxepin (DEDO)
62.7 g of the compound of formula

(101a) 

are suspended in a reaction vessel at room temperature under stirring in 400 g acetic acid ethyl ester. A solution of 44.4 g dicyclohexylcarbodiimid, dissolved in 200 g acetic acid ethyl ester is mixed in this suspension. The temperature rises up to about 30°C. The suspension is stirred vigorously at room temperature during about 10 hours and filtered afterwards. After evaporation the pure product of formula

(101) 

is obtained by crystallization from a mixture of acetic acid ethyl ester (60g)/cyclohexan (220g) as yellow crystals.

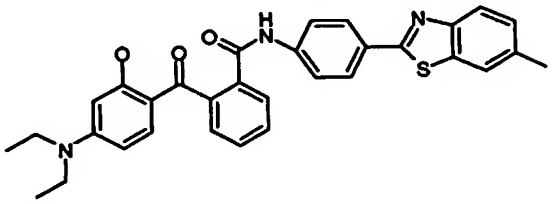
Yield: 42 g

Fp: 83.5°C

Analyses: C,H,N content corresponds to the theory values; H-NMR ; C-NMR ;
MS confirms the oxepin structure.

Analogous to this procedure the compounds can be obtained by dehydratisation of BB-acid with acetic anhydride instead of dicyclohexyl carbodiimide.

Example 2: Preparation of the compound of formula

(102) 

7.2 g of 2-(4-aminophenyl)-6-methyl-benzothiazol are suspended in 60 ml diethylenglycol-dimethylether at room temperature. A solution of 10.6g of the compound of formula (101), dissolved in 20 ml diethylenglycol-dimethylether, are added under stirring and the reaction mass is heated up 90°C. After a reaction time of 4 hours the reaction mass is cooled down to room temperature and the raw product is filtered off. The pure compound is obtained by extraction of the raw product with ethanol.

Yield : 7.3 g beige powder

Fp: 225°C

C= 71.6% ;H =5.2% ; N = 7.8% ; S = 5.96 %

All values correspond with theory.

UV spectrum in dioxan:

1.Maximum at 336 nm e= 57318

2.Maximum at 360 nm e = 49032

Example 3: Preparation of a dispersion with active content of 38 %:

In Dispermat LC equiped with 19.3g grinding pearls ER 120 S, 0.3-0.4 mm

3.4g of the compound of formula (102)

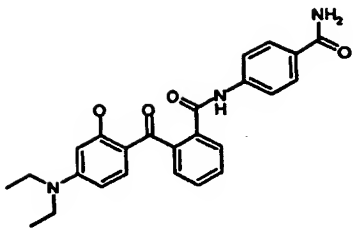
0.3g Arlacel P 135 and

5.3g Crodamol AB

are grinded during 4.5 hours. A very fine grinded dispersion is obtained which has a SPF value of 16.4.

This dispersion covers very good a broad UV-rang (320 - 380 nm)

Example 4: Preparation of the compound of formula (103)



6 g of the compound of formula (101) are dissolved in 40 ml Dioxan. 2.5 g 4-aminobenzamide are added to this solution while stirring. After a reaction time of 2 hours at 85°C dioxan is removed under vacuum and the residue is worked up by recrystallization from 2-methoxyethanol to the pure product.

Yield: 3 g white crystals

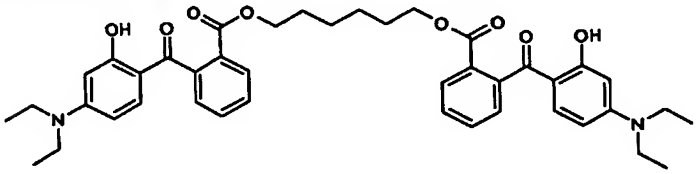
Fp 254°C

Elemental analysis: C,H,N content corresponds to the theory.

UV-Spectrum in dioxan:

Maximum at 358 nm ; e= 34848

Example 5: Preparation of the compound of formula (104)



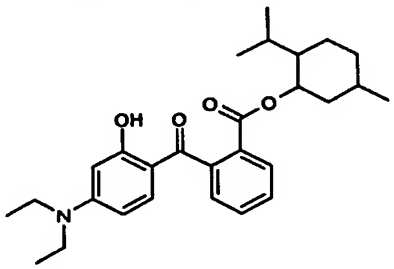
2.36 g 1,6-hexandiol, 6g toluene and 11.8g of the compound of formula (101) are stirred during 5 hours at 110°C.

Afterwards toluene is distilled off and the distilled residue is recrystallized from acetone.

Yield: 7.2 g white crystals

Fp: 148°C

Example 6: Preparation of the compound of formula

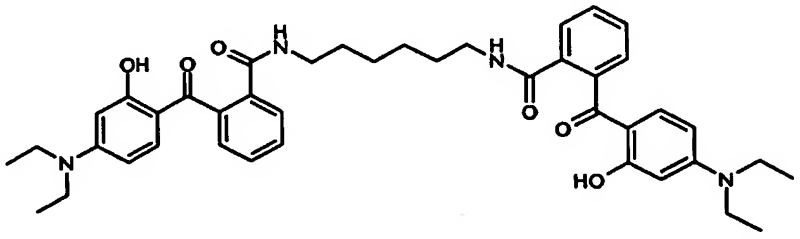
(105) 

9.2 g of the compound of formula (101), 14.4g of the racemic mixture of menthol, 18 ml of diethylenglycol-dimethylether, 0.1g of 1.8-diazabicyclo(5.4.0)-undec-7-ene(1,5,5) are stirred at 100°C during 2 hours. Then the solvent is resolved in vacuum and the residue separated with column chromatographic methods (Kieselgel 60/Toluene–acetic acid ester 8:2).
Yield: 12.8g of a glassy non-crystalline mass
Analyses: C/H/N = 74.5%/8.4%/3.04% corresponding to the theory.

UV Spectrum in dioxan:

Maximum at 351 nm; e=38565

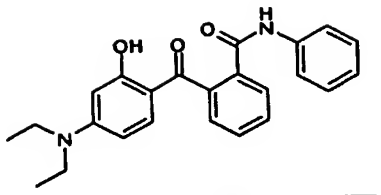
Example 7: Preparation of the compound of formula

(106) 

6 g of the compound of formula (101) are dissolved in 30 ml dioxan at room temperature. 1.16 g 1.6-diaminohexane, dissolved in 20 ml dioxan are added to this solution under stirring. Stirring of the reaction masse at room temperature is continued during 12 hours, then dioxan is removed in the vacuum and the raw product is recrystallized after extraction with water from methanol.
Yield: 4.2 g , yellow crystals
Fp: 160°C

Elemental analysis corresponds to the theoretical values.

Example 8: Preparation of the compound of formula (107)



9 g of the compound of formula (101) and 8.4g aniline are dissolved in 18 ml diethylenglycol-dimethylether. The reaction is warmed up to 70°C and stirred at this temperature for 3 hours. After evaporation of the reaction mass in vacuum the pure product is obtained after recrystallization from methanol.

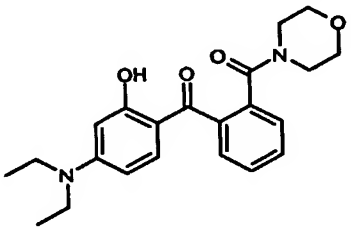
Yield: 6.2 g yellow crystals

Fp: 152°C

UV Spektrum (in Dioxan)

Maximum at 359 nm ; e = 34724

Example 9: Preparation of the compound of (108)



7.4 g of the compound of formula (101) are dissolved in 25 ml dioxan. 3.3 g morpholine dissolved in 10 ml dioxan are stirred into this solution. The reaction mass is stirred during about 20 hours at room temperature, the reaction mixture is evaporated in vacuum and the pure poduct is recrystallized from acetic acid ethyl ester.

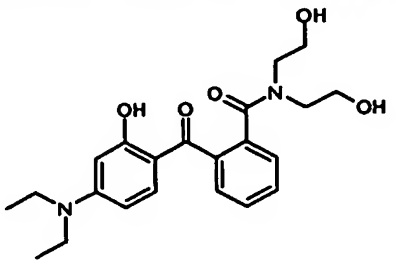
Yield: 7.5 g yellow crystals;

Fp. 155°C

UV Spectrum (in dioxan):

Maximum at 360 nm; e = 37900

Example 10: Preparation of the compound of formula

(109) 

9 g of the compound of formula (101), 9.5 g diethanolamine, dissolved in 30 ml diehylenglycol-dimethylether are stirred at 85°C during 3 hours. The reaction mass is narrowed in vacuum (0.03 mB/70°C). The residue is extracted with ca. 250 ml water at 70°C. The pure compound recrystallizes from the aqueous phase after cooling down.

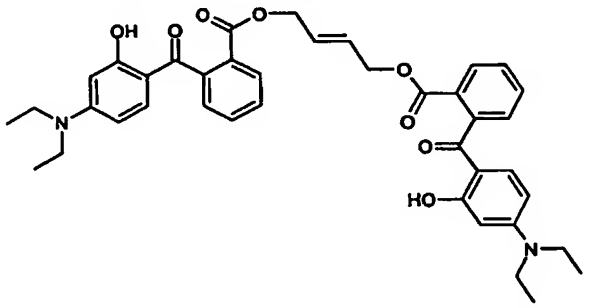
Yield: 2.1g yellow crystals;

Fp. 141°C

UV spektrum (in dioxan):

Maximum at 359 nm; e = 35080

Example 11: Preparation of the compound of formula

(110) 

125.2 g 4-diethylamino-2-hydroxy-benzophenone-carbon acid (BB-acid)

700 ml acetic acid ethyl ester,

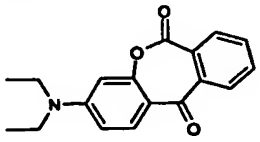
38.8 g potassium crbonate; and

53.1 g acetanhydride

are stirred intensively during 16 hours at room temperature.

Then the reaction mixture is filtered off and the filtrate is evaporated to a weight of 157 g.

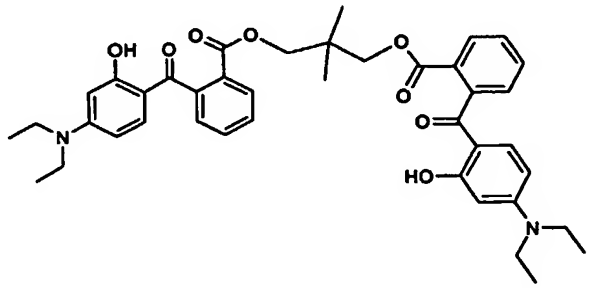
The anhydroform of the BB-acid (DEDO) recrystallizes from the vaporization residue

(101) 

Yield: 99 g (yellow crystals, Fp=82°C)

The crystals are dissolved in
18 g diethylenglykol-dimethylether,
14.6 g 2-Buten-1,4-diol is added and 1.1g 4-dimethylamino-pyridine is added under stirring at 110°C to the di-Ester (compound of formula (110)).
A quantitative yield is obtained.
The pure compound is obtained by column chromatographic methods – Kieselgel 60 / diluent: Toluene acetic acid ethyl ester / 8:2.
The pure product in shred form is an amorphous yellow powder.
It has a good solubility for example in Finsolve TN (C 12-15 alkylbenzoate) > 10%.
UV-Spectrum in Dioxan: Max. 351 nm, mol Ext. 65551

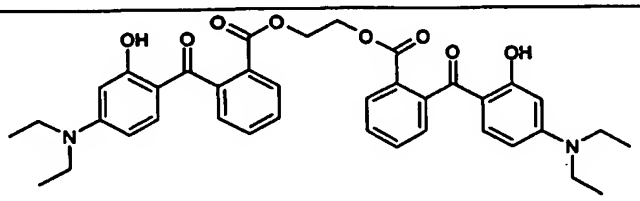
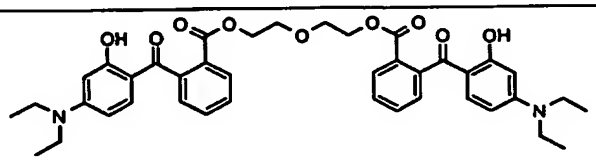
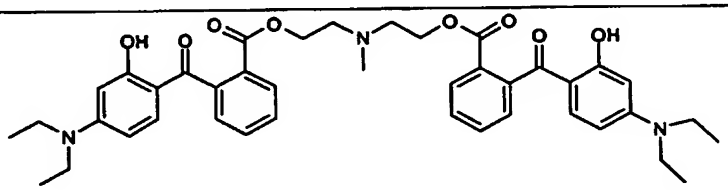
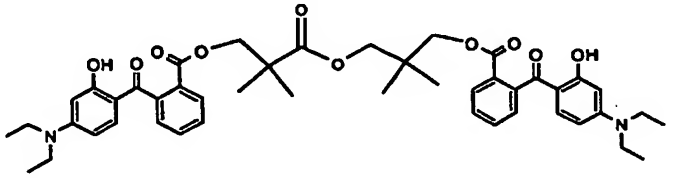
Example 12: Preparation of the compound of formula

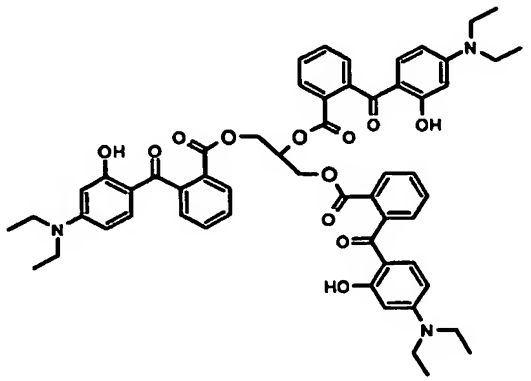
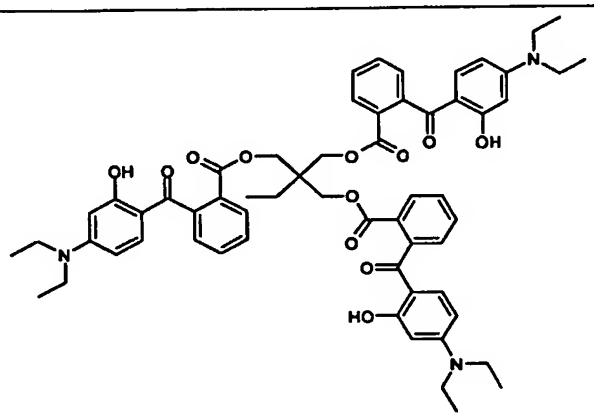
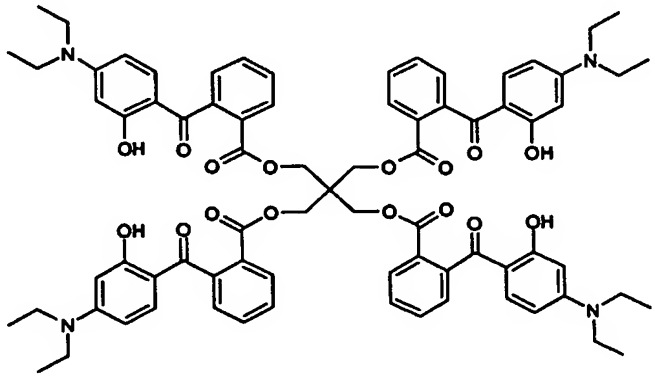
(111) 

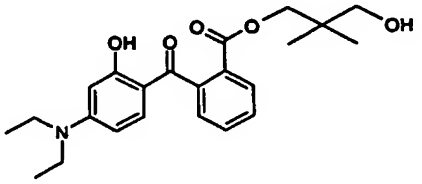
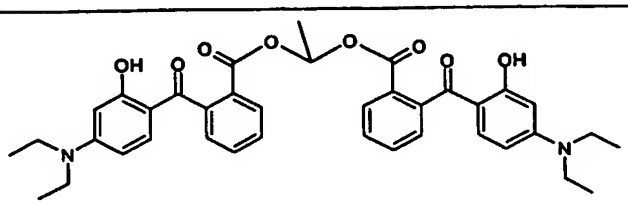
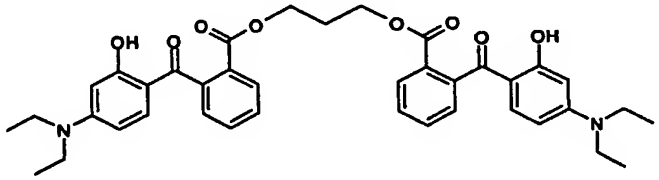
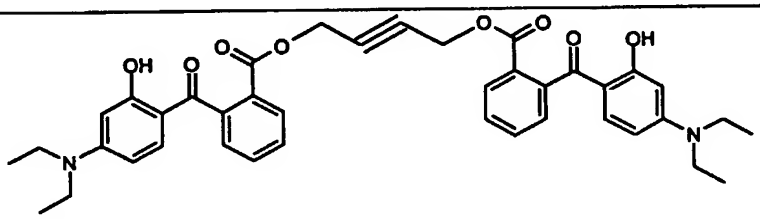
Analogous to example 11 17.3g 2,2-Dimethyl-1,3-propandiol instead of 2-buten-1,4-diol are reacted with the anhydrous form of the BB-acid.
The working up of the raw product can be carried out according to the methods as described above.
The obtained compound is an amorphous, yellow powder
Solubility in Finsolve TN > 30%
UV Spectrum in Ethanol: Max. 354 nm , mol. Ext. 65296

Examples 13 to 23: Preparation of further hydroxyphenyl benzophenone derivatives

According to the method as described in Example 11 the follwing compounds can be prepared:

Example	Compound of formula	Structure
13	112	
14	113	
15	114	
16	115	

Example	Compound of formula	Structure
17	116	
18	117	
19	118	

Example	Compound of formula	Structure
20	119	
21	120	
22	121	
23	122	

Application Examples

Example 24: Preparation of a Sun Screen agent

Sinnowax AO	7g
Cerasynt SD-V	2g
Cetylalcohol	1.5g
Dow Corning 200 Fluid	1g
Witconol TN	15g
Compound of formula (110)	2g
Octyl Triazone	2g
Butyl Methoxydibenzoylmethane	1.5g

Glycerin	10g
EDTA	0.2g
Preservative/water deion.	Exp. 100g

Example 25: Preparation of a Sunscreen Formulation

SINNOWAX AO	7g
Cerasynt SD-V	2g
Cetylalcohol	1.5g
Dow Corning 200 Fluid Witconol	1g
Witconol TN	15g
Octyl Triazone	2g
Butyl Methoxydibenzoylmethane	2g
Parsol 1789 (Hoffman-La Roche)	1.5g
Glycerin	10g
Compound of formula (111)	2g
Preservative/Water deion.	Exp. 100g

Example 26: Preparation of a sunscreen formulation

Arlacel 165 FL	2g
Stearylalcohol	1g
Stearine TP	2.5g
Dow Corning 200 Fluid	0.5g
Witconol TN	15g
Triethanolamin	0.5g
Compound of formula (111)	1.5g
Octyl Triazone	2g
Butyl Methoxydibenzoylmethane	1g
Glycerine	5g
Amphisol K	1g
Synhalen K	0.3g
Methocel F4M EDTA	0.1g
Triethanolamine	0.2g
Preservative/ waterer deion.	auf pH = 7
	exp. 100g

Example 27: O/W Emulsion

(A):

Compound of formula (110) or (111)	3 g
Sesame Oil	10 g
Glyceryl Stearate	4 g
Stearic Acid	1 g
Cetyl Alcohol	0.5 g
Polysorbate 20	0.2 g

(B):

Propylene Glycol	4 g
Propylparabene	0.05 g
Methylparabene	0.15 g
Triethanolamine	0.1 g
Carbomer 934	0.1 g
Water	ad 100 ml

Preparation of the emulsion

Phase (A):

Firstly, the UV absorber is dissolved in sesame oil. The other components of (A) are added thereto and combined.

Phase (B):

Propylparabene and methylparabene are dissolved in propylene glycol. 60 ml of water are then added, heating to 70°C is carried out and then carbomer 934 is emulsified therein.

Emulsion:

(A) is slowly added to (B) with vigorous application of mechanical energy. The volume is adjusted to 100 ml by the addition of water.

Example 28: Daily care cream, type O/W

	INCI name	% w/w (as used)
Part A	Glyceryl stearate (and) cetearyl alcohol (and) cetyl palmitate (and) cocoglycerides	4.0
	Ceteareth-12	4.0
	Cetearyl alcohol	2.0
	Dicaprylyl ether	4.5
	Ethylhexyl stearate	4.0
	Hexyl laurate	3.5
	Ethylhexyl triazone	1.0
	Benzylidene malonate polysiloxane	2.0
	HDI/trimethylol hexyl-lactone crosspolymer (and) silica	5.0
	Stearyl dimethicone	1.0
	Dimethicone	2.0
	Cetyl alcohol	0.8
	Compound of formula (110) or (111)	2.0
Part B	Water	q.s. to 100
	Water (and) scleroglucan (and) phenoxyethanol	2.0
	Glycerol	2.0
Part C	Steareth-10 allyl ether/acrylate copolymer	0.45
	Phenoxyethanol (and) methylparabene (and) ethylparabene (and) butylparabene (and) propylparabene (and) isobutylparabene	0.7
Part D	Aqua (and) tocopheryl acetate (and) caprylic/capric triglyceride (and) polysorbate 80 (and) lecithin	4.0
Part E	Water (and) sodium hydroxide	q.s.
	Fragrance	q.s.

Preparation procedure:

Part A and part B are heated separately to 80°C. Part A is poured into part B, whilst stirring continuously. Afterwards the mixture is homogenized with an Ultra Turrax at 11 000 rpm for 20 sec.. The mixture is cooled to 60°C and part C is added. At a temperature below 30°C, part D is added and the pH value is adjusted with sodium hydroxide to between 6.5 and 7.0. Finally, fragrance is added.

Example 29: Sun-protection cream, type O/W

	INCI name	% w/w (as used)
Part A	Polyglyceryl-3 methylglucose distearate	2.0
	Decyl oleate	5.7
	Isopropyl palmitate	5.8
	Caprylic/capric triglyceride	6.5
	Compound of formula (110) or (111)	2.0
	Ethylhexyl methoxycinnamate	5.0
	Cetyl alcohol	0.7
Part B	Glycerol	3.0
	Carbomer	0.3
	Water	q.s. to 100
Part C	Phenoxyethanol (and) methylparabene (and) ethylparabene (and) butylparabene (and) propylparabene (and) isobutylparabene	0.5
Part D	2,2'-Methylene-bis-(6-(2H-benzotriazole-2-yl)-4-(1,1,3,3-tetramethylbutyl)-phenol (Tinosorb M) (and) aqua (and) decyl glucoside (and) propylene glycol (and) xanthan gum	8.0
	Water	20.0
Part E	Water (and) sodium hydroxide	q.s.
	Fragrance	q.s.

Preparation procedure

Part A and part B are heated separately to 75°C. Part A is poured into part B whilst stirring. The mixture is homogenised with an Ultra Turrax at 11 000 rpm for 15 sec. The mixture is cooled to 60°C and part C and part D are incorporated. The mixture is homogenised again for a short time (5 sec./11 000 rpm) and further cooled, with moderate stirring. At room temperature, the pH is adjusted with sodium hydroxide solution to between 5.5 and 6.0. Finally, fragrance is added.

Example 30: Daily Care UV-protection Lotion

	INCI name	% w/w (as used)
Part A	Oleth-3 phosphate	0.6
	Steareth-21	2.5
	Steareth-2	1.0

	INCI name	% w/w (as used)
	Cetyl alcohol	0.8
	Stearyl alcohol	1.5
	Tribehenin	0.8
	Isohexadecane	8.0
	Compound of formula (110) or (111)	5.0
Part B	Water	q.s. to 100
	Glycerol	2.0
	2,2'-Methylene-bis-(6-(2H-benzotriazole-2-yl)-4-(1,1,3,3-tetramethylbutyl)-phenol (Tinosorb M) (and) aqua (and) decyl glucoside (and) propylene glycol (and) xanthan gum	3.0
	Disodium EDTA	0.1
Part C	Water	20.0
	Diazolidinyl urea (and) iodopropynyl butylcarbamate	0.15
	Propylene glycol	4.0
Part D	Sodium acrylate copolymer (and) liquid paraffin (and) PPG-1 trideceth-6	1.5
	Cyclopentasiloxane	4.5
	PEG-12 dimethicone	2.0
	Tocopheryl acetate	0.45
	Water (and) citric acid	q.s.
Part E	Fragrance	q.s.

Preparation procedure

Heat part A and part B separately to 75°C. Pour part A into part B, whilst stirring continuously. Immediately after emulsification, incorporate in the mixture SF 1202 and SF 1288 from part D. Afterwards homogenise with an Ultra Turrax at 11 000 rpm for 30 sec.. Allow to cool to 65°C and incorporate SALCARE® SC91. At a temperature below 50°C, add part C. At 35°C or below, incorporate vitamin E acetate and subsequently adjust the pH with citric acid. At room temperature, add part E.

Example 31: Sun-protection Cream, type O/W

	INCI name	% w/w (as used)
Part A	Polyglyceryl-3 methylglucose distearate	2.0
	Decyl oleate	5.7

	INCI name	% w/w (as used)
	Isopropyl palmitate	5.8
	Caprylic/capric triglyceride	6.5
	Compound of formula (110) or (111)	2.0
	Ethylhexyl methoxycinnamate	5.0
	Cetyl alcohol	0.7
Part B	Glycerol	3.0
	Carbomer	0.3
	Water	q.s. to 100
Part C	Phenoxyethanol (and) methylparabene (and) ethylparabene (and) butylparabene (and) propylparabene (and) isobutylparabene	0.5
Part D	2,2'-Methylene-bis-(6-(2H-benzotriazole-2-yl)-4-(1,1,3,3-tetramethylbutyl)-phenol (and) aqua (and) decyl glucoside (and) propylene glycol (and) xanthan gum	8.0
	Water	20.0
Part E	Water (and) sodium hydroxide	q.s.
	Fragrance	q.s.

Preparation procedure:

Part A and part B are heated separately to 75°C. Part A is poured into part B whilst stirring. The mixture is homogenised with an Ultra Turrax at 11 000 rpm for 15 sec.. The mixture is cooled to 60°C, and part C and part D are incorporated. The mixture is homogenised again for a short time (5 sec./11 000 rpm). After further cooling, with moderate stirring, the pH is adjusted with sodium hydroxide at room temperature. A solution between pH 5.50 and 6.00 is obtained. Finally, fragrance is added.

Example 32: Sun-protection Cream, type O/W

	INCI name	% w/w (as used)
Part A	Polyglyceryl-3 methylglucose distearate	2.0
	Decyl oleate	5.7
	Isopropyl palmitate	5.8
	Caprylic/capric triglyceride	6.5
	Mixture of the Compound of formula (110) or (111) (50 %) and Uvinul A Plus CAS Reg. No. 302776-68-7 (50 %)	2.0
	Ethylhexyl methoxycinnamate	5.0

	INCI name	% w/w (as used)
	Cetyl alcohol	0.7
Part B	Glycerol	3.0
	Carbomer	0.3
	Water	q.s. to 100
Part C	Phenoxyethanol (and) methylparabene (and) ethylparabene (and) butylparabene (and) propylparabene (and) isobutylparabene	0.5
Part D	2,2'-Methylene-bis-(6-(2H-benzotriazole-2-yl)-4-(1,1,3,3-tetramethylbutyl)-phenol (and) aqua (and) decyl glucoside (and) propylene glycol (and) xanthan gum	8.0
	Water	20.0
Part E	Water (and) sodium hydroxide	q.s.
	Fragrance	q.s.

Preparation procedure:

Part A and part B are heated separately to 75°C. Part A is poured into part B whilst stirring. The mixture is homogenised with an Ultra Turrax at 11 000 rpm for 15 sec.. After cooling 60°C, part C and part D are incorporated. The mixture is homogenised again for a short time (5 sec./11 000 rpm). After further cooling, with moderate stirring, the pH is adjusted at room temperature with sodium hydroxide solution to between 5.50 and 6.00. Finally, fragrance is added.